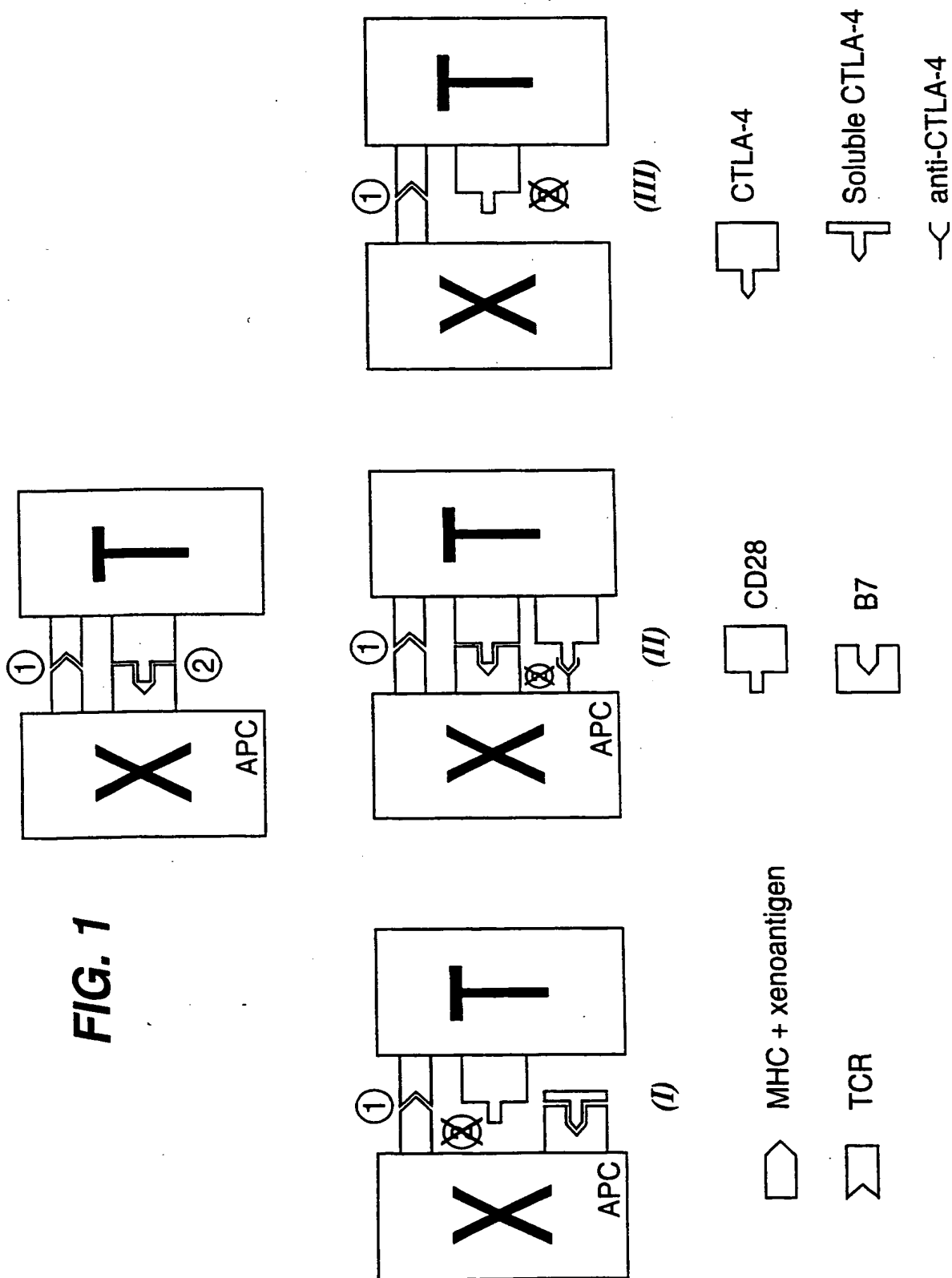


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361 371 381 391 401 411
 GCCGTGGACA CTGGGCTCTA CATCTGCAAG GTGGAGCTCC TGTACCCACC ACCCTACTAT
 ..A.....G..A..... ..A.....G..A.....
 ..A.....TG.....A.....G..A.....

421 431 441 451 461 471
 GTGGGTATGG GCAACGGGAC CCAGATTAT GTCATTGATC CAGAACCATG CCCAGATTCT
 C....C..A.....AG.....A.....G.....
C..C.....T..A.....C.....G.....

481 491 501 511 521 531
 GATTTCCTGC TCTGGATCCT GGCAGCAGTT AGTTCAGGGT TGTTTTITTA CAGCTTCCTC
 ..C.....C.....T.....G.....T.....
T..C..... ..C.....

541 551 561 571 581 591
 ATCACAGCTG TTTCTTTGAG CAAAATGCTA AAGAAAAGAA GTCCTCTTAC TACAGGGGTC
 C..... ..C..... ..C.....

601 611 621 631 641 651
 TATGTGAAA TGCCTCCGAC AGAGCCAGAA TGTGAAAAGC AATTTCAGCC TTATTTTATT
A.....
A.....

661 671
 CCCATCAATT GA

SEQ ID: 2 (pCTLA4)
 Human CTLA4
 Cattle CTLA4

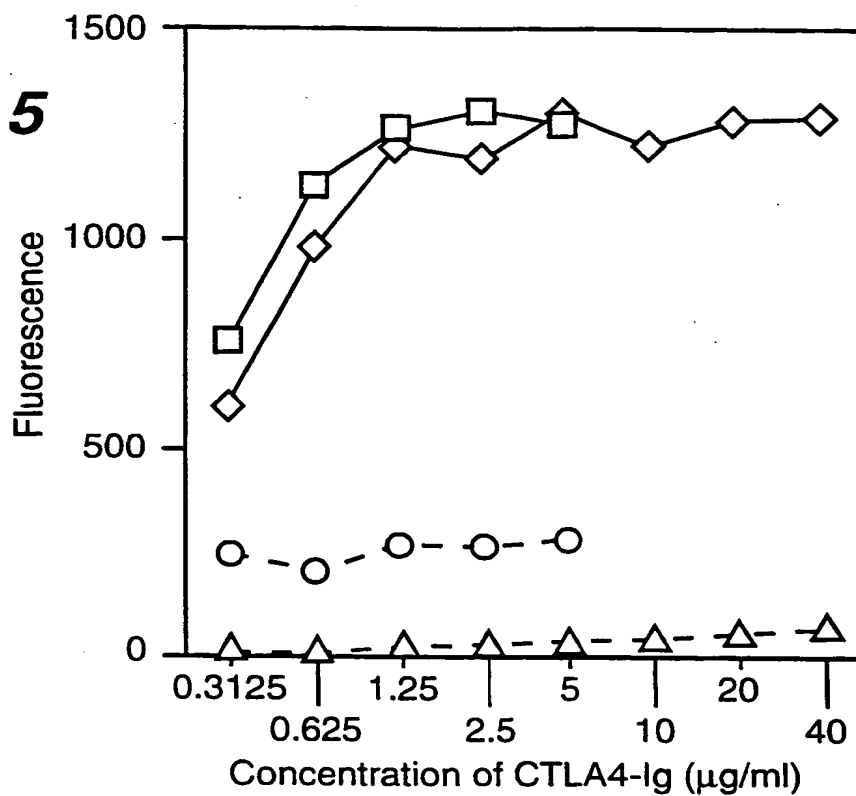
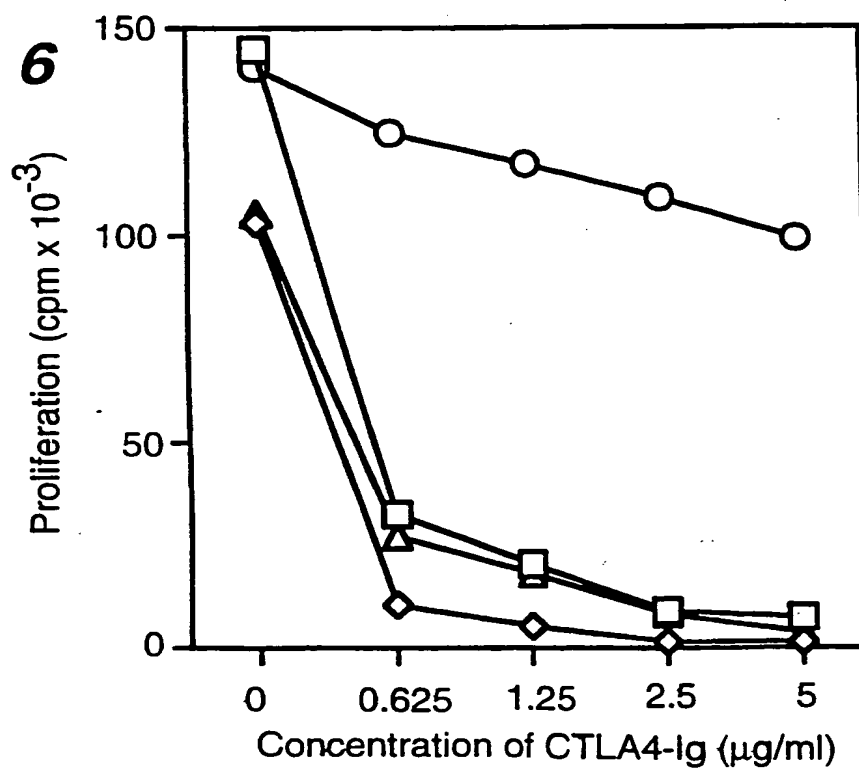
FIG. 3 (CONTD.)

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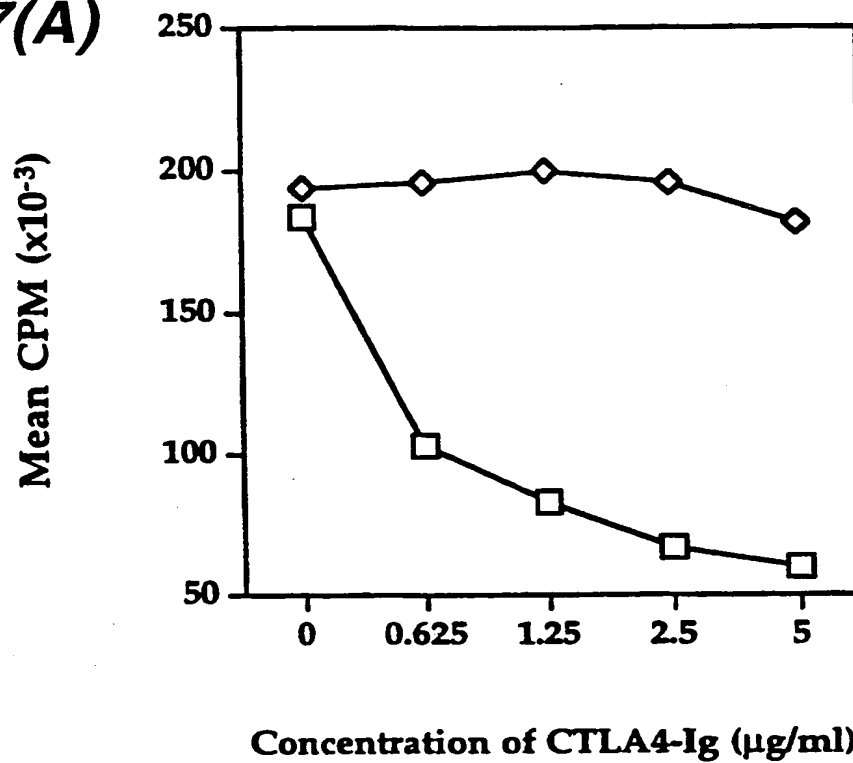
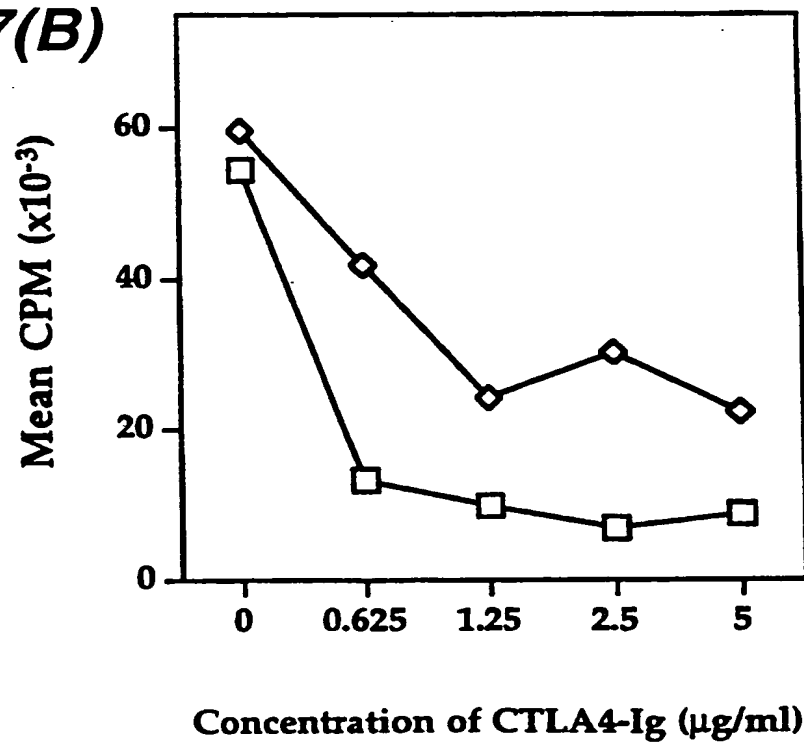
FIG. 4

-30	-20	-10	1	11	21
MACSGFRSHG	AWLELTSRTW	PCTALFSLLF	IPVFSKGMHV	AQPAVVLANS	RGVASFVCEY
31	41	51	61	71	81
GSAGKAAEVR	VTVLRRAGSQ	MTEVCAATYT	VEDELTFLDD	STCTGTSTEN	KVNLTIQGLR
91	101	111	121	131	141
AVDTGLYICK	VELLYPPPY	VGMNGTQIY	VIDPEPCPDS	<u>DGGSGGAAEP</u>	KSCDKTHTCP
151	161	171	181	191	201
PCPAPELLGG	PSVFLFPPKP	KDTLMIS RTP	EVTVCVVVDVS	HEDPEVKFNW	YVDGVEVHNA
211	221	231	241	251	261
KTKPREEQYN	STYRVVSVLT	VLHQDWLNGK	EYKCKVSNKA	LPAPIEKTIS	KAKGQPREPQ
271	281	291	301	311	321
VYTLPPSRDE	LTKNQVSLTC	LVKGFYPSDI	AVEWESNGQP	ENNYKTTPPV	LDSDGSFFLY
331	341	351	361		
SKLTVDKSRW	QQGNVFCSCV	MHEALHNHYT	QKSLSLSPGK		

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FIG. 5**FIG. 6**

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FIG. 7(A)**FIG. 7(B)**

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FIG. 8

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1..... 11..... 21..... 31..... 41..... 51..... 61..... 71.....
CCGAGGTGCA GCTGGTGGAG TCTGGGGGAG GCTTGGTACA GCCTGGGGGG TCCCTGAGAC TCTCCTGTGC AGCCTCTGGA

81..... 91..... 101..... 111..... 121..... 131..... 141..... 151.....
TTCACCTTTA GCAGCTATGC CATGAGCTGG GTCCGCCAGG CTCACGGGAA GGGGCTGGAG TGGTCTCAG CTATTAGTGG

161..... 171..... 181..... 191..... 201..... 211..... 221..... 231.....
TAGTGGTGGT AGCACATACT ACGCAGACTC CGTGAAGGCG CGGTTACCCA TCTCCAGAGA CAATCCAAAG AACACGCTGT

241..... 251..... 261..... 271..... 281..... 291..... 301..... 311.....
ATCTGCAAT GAACAGCCTG AGAGCCGAGG ACACGGCCGT GTATTACTGT GCAAGAGCTG GTCGTATTTT GTTTGACTAT

321..... 331..... 341..... 351..... 361..... 371..... 381..... 391.....
TGGGGCCAAG GTACCCCTGGT CACCGTCTCG AGTGGTGGAG GCGGTTCAGG CGGAGGTGGC TCTGGCGGTA GTGCACTTCA

401..... 411..... 421..... 431..... 441..... 451..... 461..... 471.....
GTCTGTGCTG ACTCAGCCAC CCTCAGCGTC TGGGACCCCC GGGCAGAGGG TCACCATCTC TTGTTCTGGA AGCAGCTCCA

481..... 491..... 501..... 511..... 521..... 531..... 541..... 551.....
ACATCGGAAG TAATTATGTA TACTGGTACC AGCAGCTCCC AGGAACGGCC CCCAACTCC TCATCTATAG GAATAATCAG

561..... 571..... 581..... 591..... 601..... 611..... 621..... 631.....
CGGCCCTCAG GGTCCCTGA CCGATTCTCT GGCTCCAAGT CTGGCACCTC AGCCTCCCTG GCCATCAGTG GGCTCCGGTC

641..... 651..... 661..... 671..... 681..... 691..... 701..... 711.....
CGAGGATGAG GCTGATTATT ACTGTGCAGC ATGGGATGAC AGCCTGGTAT TCGGCGGAGG GACCAAGCTG ACCGTCCTAG

721
GT

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FIG. 9

1..... 11..... 21..... 31..... 41..... 51..... 61..... 71.....
EVOLVESGGG LVQPGGSLRL SCAASGETFS SYAMSWVRQA PGKGLEWVSA ISGGGGSTYY ADSVKGRFTI SRDNSKNTLY

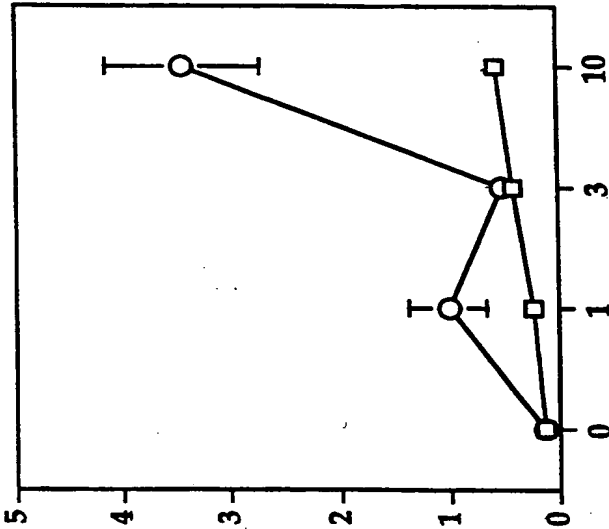
81..... 91..... 101..... 111..... 121..... 131..... 141..... 151.....
LQMNLSRAED TAVYYCARAG RILEFDYWGQG TLVTVSSGGG GSGGGGSGGS ALQSVLTQPP SASGTPGQRV TISCSGSSSN

161..... 171..... 181..... 191..... 201..... 211..... 221..... 231.....
IGSNYVYWYQ QLPGTAPKLL IYRNNQRPSG VPDRFSGSKS GTSASLAISG LRSEDEADYY CAWDDSLVF GGTGKLTVLG

LINKER

c.p.m. ($\times 10^{-3}$)

FIG. 13



Stimulators ($\times 10^{-4}$)

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FIG. 10

	10	20	30	40	50	60	
M1 sFv	CATGG-CCGAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAG						
M3 sFv	CATGG-CCCAGGTGCAGCTGCAGGAGTGGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTGTC						
M19 sFv	CATGG-CCCAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAGGCCTGGGGCCTCAGTGAA						
M24 sFv	CATGGGGCCAGGTGCAGCTGTTGCAGTCTGCAGCAGAGGTGAAAAAGCCCCGGGAGTCTCTGAA						
	70	80	90	100	110	120	
M1 sFv	ACTCTCCTGTGCAGCCTCTGGATTACCTTTAGCAGC--TA--TGCCAT--GAGCTGGGTCCGC						
M3 sFv	CCTCACCTGCACTGTCTCTGGTGGCTCCGTCAGCAGTGGTAGTTACTACTGGAGCTGGATCCGG						
M19 sFv	GGTTTCCTGCAAGGCATCTGGATACACCTTCACCAGC-----TACTATATGCACTGGGTGCGA						
M24 sFv	GATCTCCTGTAAGGGTTCTGGATACAGCTTTACCAGC-----TACTGGATCGGCTGGGTGCCG						
	130	140	150	160	170	180	190
M1 sFv	CAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGGTAGTGGTGGTAGCACATACT						
M3 sFv	CAGCCCCCAGGGAAGGGACTGGAGTGGATT--GGGTAT-ATCTATTACAGTGGGAGCACCAACT						
M19 sFv	CAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCCTAGTGGTGGTAGCACAAAGCT						
M24 sFv	CAGATGCCCCGGGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATAACCAGAT						
	200	210	220	230	240	250	
M1 sFv	ACGCAGACTCCGTGAAGGGCCGGTTACCATCTCCAGAGACAATTCCAAGAACAGCTGTATCT						
M3 sFv	ACAACCCCTCCCTCAAGAGTCGAGTCCCATATCAGTAGACAGTCCAAGAACCAGTTCTCCCT						
M19 sFv	ACGCACAGAAGTTCCAGGGCAGAGTCCCATGACCAGGGACAGTCCACGAGCACAGTCTACAT						
M24 sFv	ACAGCCCGTCCTTCCAAGGCCAGGTACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCT						
	260	270	280	290	300	310	320
M1 sFv	GCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCAAGAGCTG-----GT						
M3 sFv	GAAGCTGAGCTCTGTGACCGCTGGGACACGGCCGTGTATTACTGTGCAAGAATGC-----GG						
M19 sFv	GGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCAAGAGTGGCTCCCTAT						
M24 sFv	GCAGTGGAGCAGCCTGAAGGCCTCGGACACGGCCGTGTATTACTGTGCAAGATT--TTGCT-T						
	330	340	350	360	370	380	
M1 sFv	CGTATTTTGTGTTGACTATTGGGGCCAAGGTACCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M3 sFv	AAGGATAAGTTTGTGACTATTGGGGCCAAGGTACCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M19 sFv	GTGAATACGCTTGTTTTTTGGGGCCAAGGTACCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M24 sFv	GGTGGT---TTTGACTATTGGGGCCAAGGTACCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						

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          390      400      410      420      430      440
          |        |        |        |        |        |
M1 sFv    CAGGCGGAGGTGGCTCTGGCGGTAGTGCACCTTCAGTCTGTGCTGACTCAG---CCACCCTCAGC
M3 sFv    CAGGCGGAGGTGGCTCTGGCGGTAGTGCACCTTCAGTCTGTGCTGACTCAG---CCACCCTCAGC
M19 sFv   CAGGCGGAGGTGGCTCTGGCGGTAGTGCACCTTCTCTGTGAGCTGACTCAG---GACCCTGCTGT
M24 sFv   CAGGCGGAGGTGGCTCTGGCGGTAGTGCACCTTGACATCCAGTTGACCCAGTCTCCATCCTTCCT

          450      460      470      480      490      500      510
          |        |        |        |        |        |        |
M1 sFv    GTCTGGGACCCCCCGGCAGAGGGTCACCATCTCTGTCTGTGGAAGCAGCTCCAACATCGGAAGT
M3 sFv    GTCTGGGACCCCCCGGCAGAGGGTCACCATCTCTGTCTGTGGAAGCAGCTCCAACATCGGAAGT
M19 sFv   GTCTGTGGCCTTGGGACAGACAGTCAGGATCACATGCCAAGGAGACAGCCTCA-----GAAGC
M24 sFv   GTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC---GGCCAGTCAGGGCATT---AGC

          520      530      540      550      560      570
          |        |        |        |        |        |
M1 sFv    AATTATGTATACTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACCTCCTCATCTATAGGAATA
M3 sFv    AATTATGTATACTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACCTCCTCATCTATAGGAATA
M19 sFv   TATTATGCAAGCTGGTACCAGCAGAAGCCAGGACAGGCCCCCTGTACTTGTTCATCTATGGTAAAA
M24 sFv   AGTTATTTAGCCTGGTATCAGCAAAAACAGGGAAAGCCCCCTAAGCTCCTGGTCTATGCTGCAT

          580      590      600      610      620      630      640
          |        |        |        |        |        |        |
M1 sFv    ATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCT
M3 sFv    ATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCT
M19 sFv   ACAACCGGCCCTCAGGGATCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTCCTT
M24 sFv   CCACCTTGCAAGTGGGGTCCCATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCT

          650      660      670      680      690      700
          |        |        |        |        |        |
M1 sFv    GGCCATCAGTGGGCTCOGGTCCGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGC
M3 sFv    GGCCATCAGTGGGCTCOGGTCCGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGC
M19 sFv   GACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTAACTCCCGGGACAGCAGT
M24 sFv   CACAATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGTCA---ACAGCTTAATAGT

          710      720      730      740      750
          |        |        |        |        |
M1 sFv    --CTG---GTATTGCGGCGGAGGGACCAAGCTGACCGTCTAGGTGC
M3 sFv    --CTGT-TTGTATTGCGGCGGAGGGACCAAGCTGACCGTCTAGGTGCGGCGGC
M19 sFv   GGTTTTACTGTATTGCGGCGGAGGGACCAAGCTGACCGTCTAGGTGC
M24 sFv   TACCGCTTGACGTTGCGCCAAGGGACCAAGCTGGAAATC--AAACGTG----C

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FIG. 10 (CONTD.)

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FIG. 11

10 20 30 40 50 60

M1 sFv Peptide --EVQLVESGGGLVQPGGSLRLSCAASG--FTFSSYAMSWRQAPGKLEWWSAISGSGG
M3 sFv Peptide MAQVQLQESGFGFLVKPSETLSLTCTVSGGSVSSGSYYWSWIROPFGKLEWIGYTY-YSG
M19 sFv Peptide --QVQLVQSGAEVKRPGASVKVSCKASG--YTFTSYMHWRQAPGQGLEWMGLINPSGG
M24 sFv peptide --QVQLLQSAAEVKKPGESLKLSCKGSG--YSFTSYWIGWRQMPGKLEWMGLIYPGDS

70 80 90 100 110 120

M1 sFv Peptide STYYADSVKGRFTISRDNKNIYLQMNSLRSEDITAVVYCARAGR--ILFDYWGGILVT
M3 sFv Peptide STINNPISLKSRTVLSVDTSKNQFSLKLSSVTAADTAVVYCARMRK--DKFDYWGGILVT
M19 sFv Peptide STSYAQKFQGRVIMTRDTSTSTVYMESSLRSEDITAVVYCARVAPVYNILVFWGGILVT
M24 sFv peptide DIRYSFSPFQGGVITISADKSLSTAYLQWSSLKASDTAVVYCARFS--LGGFDYWGGILVT

130 140 150 160 170 180

M1 sFv Peptide VSSGGGSGGGGSGGSALQSVLTQPPS-ASGTFQQRVTISCSGSSSNIGSNYVYWYQQLP
M3 sFv Peptide VSSGGGSGGGGSGGSALQSVLTQPPS-ASGTFQQRVTISCSGSSSNIGSNYVYWYQQLP
M19 sFv Peptide VSSGGGSGGGGSGGSALSSLTQDPA-VSVALGQTVRTTCQGDG--LRSYYASWYQQKP
M24 sFv peptide VSSGGGSGGGGSGGSALDIQLTQSPSFLSASVGLRVTITCRASQG--ISSYLAWYQQKP

190 200 210 220 230 240

M1 sFv Peptide GTAPKLLTYRNNQRPSPGVPDRFSGSKSGTSASLAIISGLRSEDEADYYCAAWDDSL--VFG
M3 sFv Peptide GTAPKLLTYRNNQRPSPGVPDRFSGSKSGTSASLAIISGLRSEDEADYYCAAWDDSLF-VFG
M19 sFv Peptide GQAPVLVIYGNRNPSPGIPDRFSGSSGNVIALITITGAQAEDEADYYCNSRDSSGFTVFG
M24 sFv peptide GKAPKLLVYAASLTQSGVPSRFSGSGGIEFTLTITSSLPQEDFATYYCQQLNSYRLT-FG

.... |
M1 sFv Peptide GGTKLTVLG
M3 sFv Peptide GGTKLTVLGAA
M19 sFv Peptide GGTKLTVLG
M24 sFv peptide QGKLEI--KR

FIG. 12

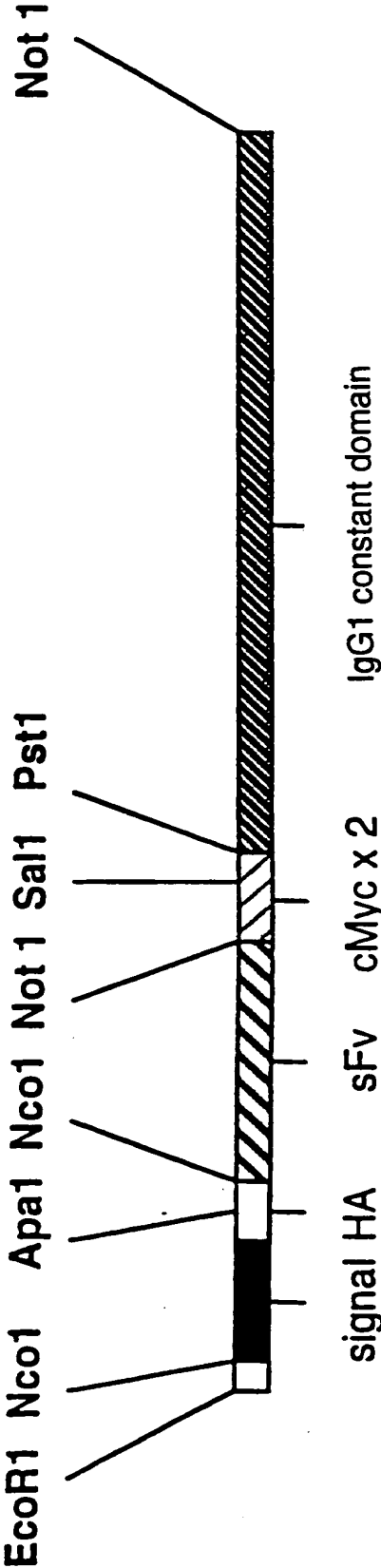
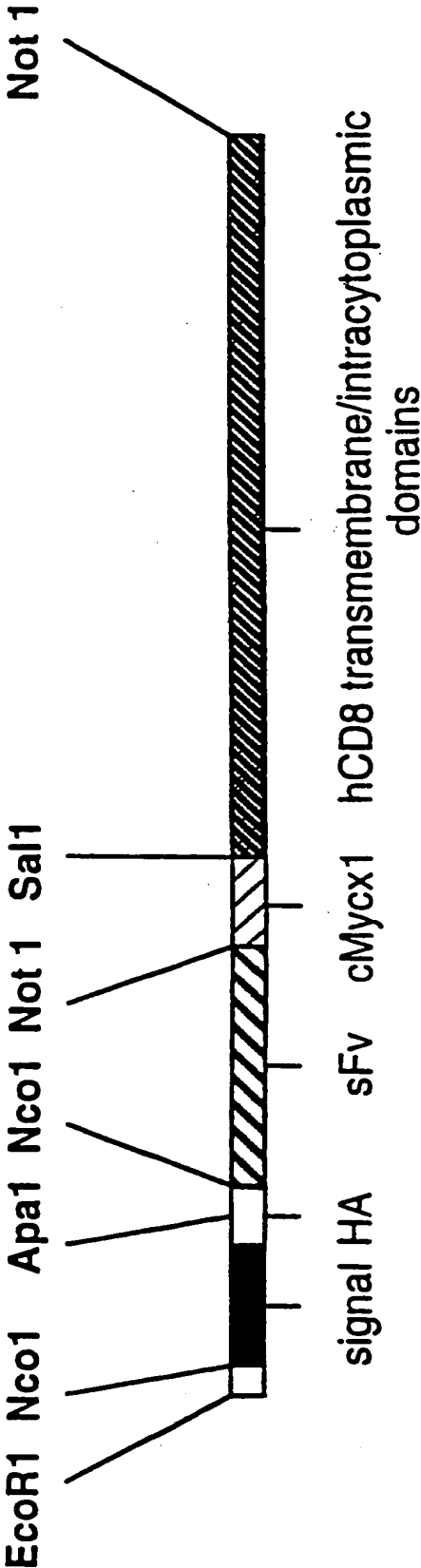


FIG. 14



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FIG. 15(A)

-65 AGCTTCAGGA TCCTGAAAGG TTTTGCTCTA CTCCTGAAG ACCTGAACAC
-15 CGCTCCCAT AAGCCATGGC TTGCCTTGA TTTCAGCGGC ACAAGGCTCA
36 GCTGAACCTG GCTACCAGGA CCTGGCCCTG CACTCTCCTG TTTTTTCTTC
86 TCTTCATCCC TGTCTTCTGC AAAGCAATGC ACGTGGCCCA GCCTGCTGTG
136 GTACTGGCCA GCAGCCGAGG CATCGCCAGC TTTGTGTGTG AGTATGCATC
186 TCCAGGCAAA GCCACTGAGG TCCGGGTGAC AGTGCTTCGG CAGGCTGACA
236 GCCAGGTGAC TGAAGTCTGT GCGGCAACCT ACATGATGGG GAATGAGTTG
286 ACCTTCCTAG ATGATTCCAT CTGCACGGGC ACCTCCAGTG GAAATCAAGT
336 GAACCTCACT ATCCAAGGAC TGAGGGCCAT GGACACGGGA CTCTACATCT
386 GCAAGGTGGA GCTCATGTAC CCACCGCCAT ACTACCTGGG CATAGGCAAC
436 GGAACCCAGA TTTATGTAAT TGATCCAGAA CCGTGCCCAG ATTCTGACTT
486 CCTCCTCTGG ATCCTTGCAG CAGTTAGTTC GGGGTTGTTT TTTTATAGCT
536 TTCTCCTCAC AGCTGTTTCT TTGAGCAAAA TGCTAAAGAA AAGAAGCCCT
586 CTTACAACAG GGGTCTATGT GAAAATGCCC CCAACAGAGC CAGAATGTGA
636 AAAGCAATT CAGCCTTATT TTATTCCCAT CAATTGAGAA TT

FIG. 15(B)

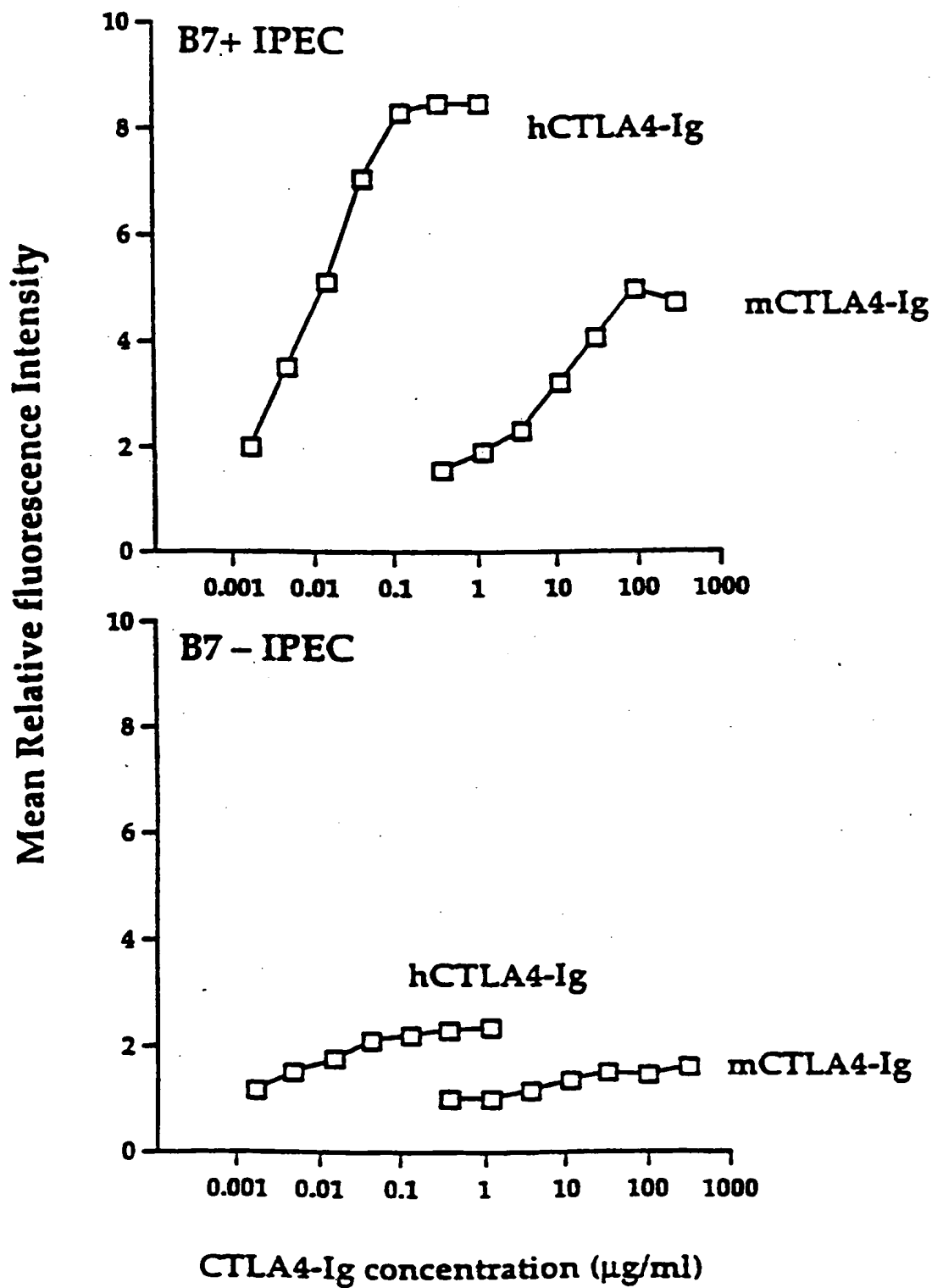
-30 -20 -10 1 11 21
MACLGFORHK AQLNLATRTW PCTLLFFLLF IPVFCAMHV AQPAAVLASS RGIASFVCEY
*
31 41 51 61 71 81
ASPGKATEVR VTVLRQADSQ VTEVCAATYM MGNELTFLDD SICTGTSSGN QVNLTIQGLR
91 101 111 121 131 141
AMDTGLYICK VELMYPPPY LGIGNGTQIY VIDPEPCPDS DFLLWILAAV SSGLFFYSFL
*
151 161 171 181
LTAVSLSKML KKRSPLETTGV YVKMPPEPE CEKQFQPYFI PIN
*

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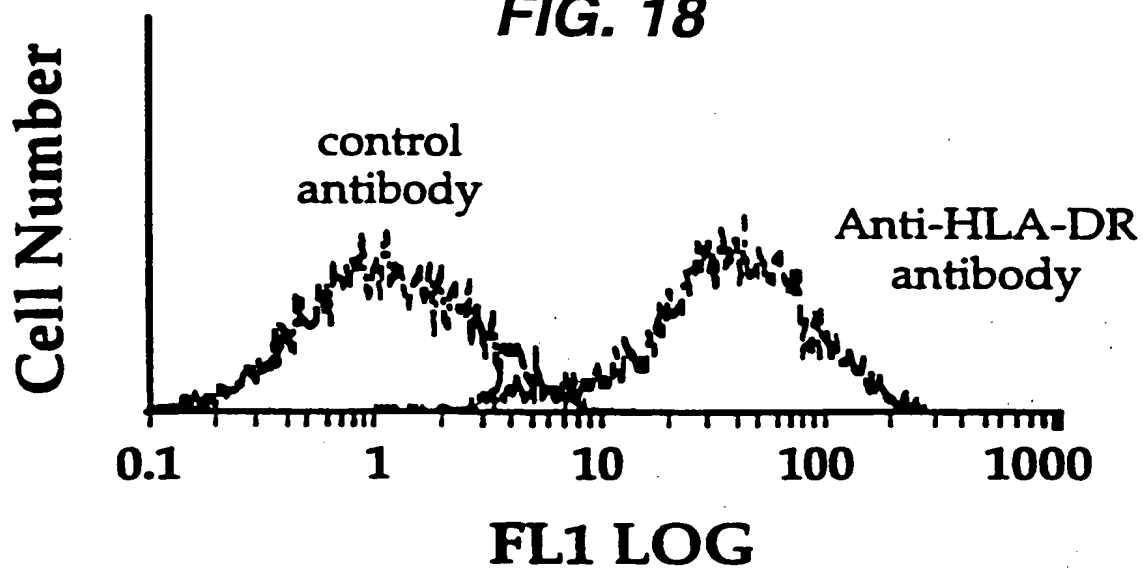
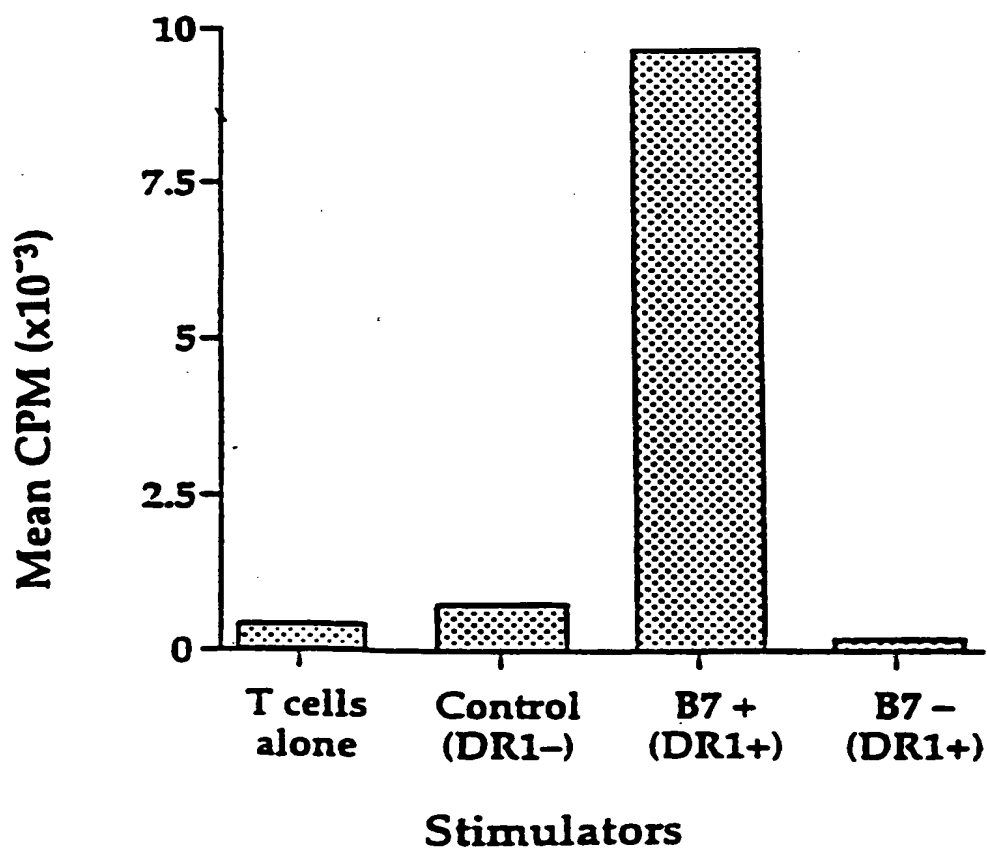
FIG. 16

-36 AAGCTTCGAG CCAAGCAGCG TCCTGGGGAG CGCGTCATGG CCTTACCAGT
15 GACCGCCTTG CTCCTGCCGC TGGCCTTGCT GCTCCACGCC GCCAGGCCGA
65 GCCAGTTCCG GGTGTCGCCG CTGGATCGGA CCTGGAACCT GGGCGAGACA
115 GTGGAGCTGA AGTGCCAGGT GCTGCTGTCC AACCCGACGT CGGGCTGCTC
165 GTGGCTCTTC CAGCCGCGCG GCGCCGCCG CAGTCCCACC TTCCTCCTAT
215 ACCTCTCCCA AAACAATCCC AAGGCGGCCA AGGGGCTGGA CACCCAGCGG
265 TTCTCGGGCA AGAGGTTGGG GGACACCTTC GTCCTCACCC TGAGCGACTT
315 CCGCCGAGAG AACGAGGGCT ACTATTTCTG CTCGGCCCTG AGCAACTCCA
365 TCATGTACTT CAGCCACTTC GTGCCGGTCT TCCTGCCAGC GAAGCCCACC
415 ACGACGCCAG CGCCGCGACC ACTAACACCG GCGCCCACCA TCGCGTCGCA
465 GCCCCTGTCC CTGCGCCCAG AGGCGTGCCG GCCAGCGGCG GGGGGCGCAG
515 TGCACACGAG GGGGCTGGAC TTCGCCTGTG ATATCTACAT CTGGGCGCCC
565 CTGGCCGGGA CTTGTGGGGT CCTTCTCCTG TCACTGGTTA TCACCCTTTA
615 CTGCAACCAC AGGAACCGAA GACGTGTTTG CAAATGTCCC CGGCCTGTGG
665 TCAAATCGGG AGACAAGCCC AGCCTTTCGG CGAGATACGT CTAACCCTGT
715 GCAACAGCCA CTACATGAAT TCC

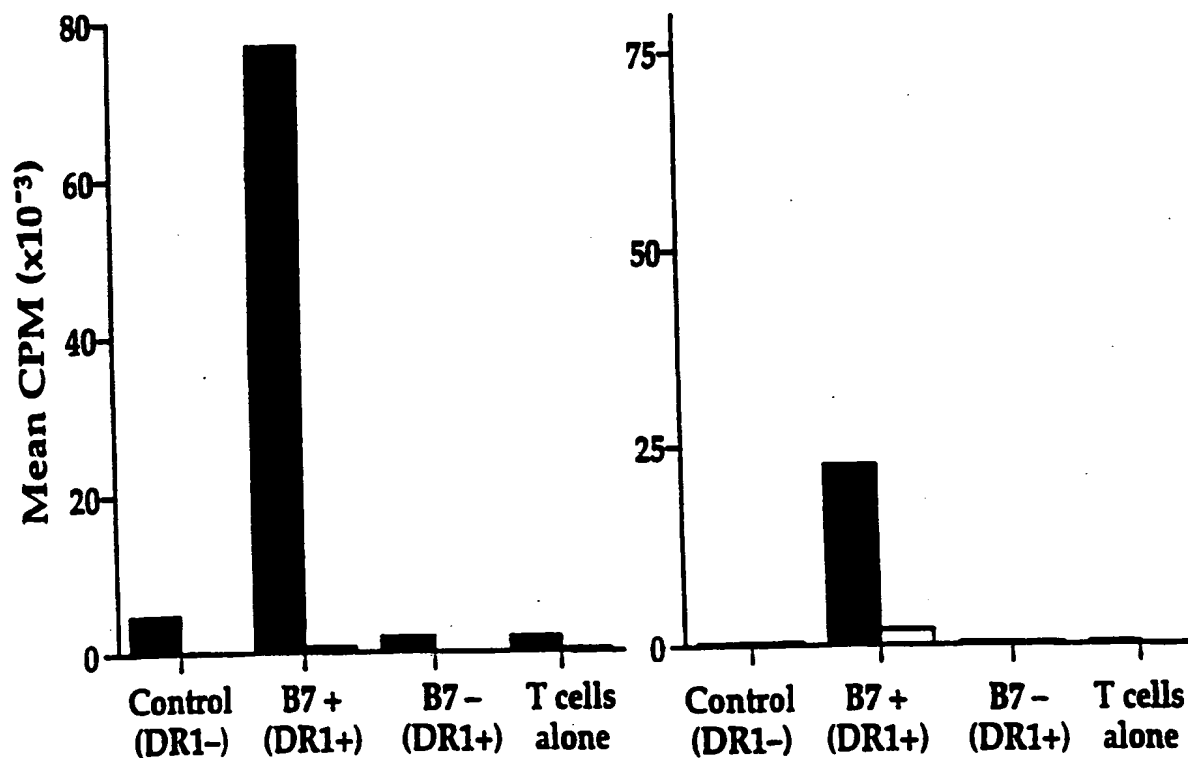
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FIG. 17

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FIG. 18**FIG. 19**

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FIG. 20**FIG. 21**